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DIAGNOSTIC AND SURGICAL PROCEDURES
IN CHRONIC PANCREATITIS
an evaluation

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an evaluation

by

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The present thesis is based on the following papers:

- I. I. Ihse, B. Arnesjö, C. Kugelberg & P. Lilja.
Intestinal activities of trypsin, lipase and phospholipase after a test meal. An evaluation of 474 examinations.
Accepted for publication in Scand. J. Gastroent.
- II. C. Kugelberg, I. Ihse, E. Cederquist, I. Larsson & U. Tylén.
An evaluation of angiography, ⁷⁵Se-methionine scintigraphy and the Lundh test in the diagnosis of pancreatic disease.
Submitted for publication in Acta Chir. Scand.
- III. B. Arnesjö, C. Kugelberg & U. Tylén.
Pancreatography in relapsing pancreatitis.
Acta Chir. Scand. 1974, 140, 131-137.
- IV. B. Arnesjö, I. Ihse, C. Kugelberg & U. Tylén.
Pancreatico-jejunostomy in chronic pancreatitis. An appraisal of 29 cases.
Acta Chir. Scand. 1975, 141, 139-148.
- V. C. Kugelberg, L. Wehlin, B. Arnesjö & U. Tylén.
Endoscopic pancreatography in evaluating results of pancreatico-jejunostomy.
Gut 1976, 17, 267-272.

The above articles will be referred to in the text by their respective Roman numerals.

"One never knows - do one?"

Fats Waller (1943)

INTRODUCTION

Chronic relapsing pancreatitis is a heavy burden to the patient, a touchstone to the physician and a challenge to the surgeon. Untreated, the condition has a lengthy clinical course, inflicting considerable pain, gastro-intestinal disorders and a general state of illness, seriously detracting from the patient's quality of life.

A wide range of clinical and pathological manifestations in a small organ situated retroperitoneally has presented great diagnostic problems. In recent years, however, experience has rapidly accumulated with new diagnostic methods and techniques in various fields of medical technology. These developments and the fact that conservative medical treatment has proved somewhat unrewarding has focused increasing surgical attention on the pancreas itself (16, 20, 27, 39, 40, 64, 79, 82). Since the disease does not present a defined consistent lesion, no standard operative procedure can be designed. The operation performed must accord with the findings in the individual patient.

Pathology

The chronic inflammatory changes are most varied. Initially there is induration and slight fibrosis which during the onset of the disease increases and is accompanied by dilatation of small ducts and the appearance of non calcified plugs. In the advanced stages the gland is often almost entirely replaced by sclerotic tissue containing dilated ducts filled with calcified plugs, or it may present more pronounced destructive changes with cellular infiltration and fat necrosis. During the course of the disease cysts, abscess formation and necrosis may occur. All these changes may be present in different parts of the gland, involve the entire organ or appear in restricted areas, leaving the remaining parenchyma intact. The inflammatory features are generally followed by changes in the duct of Wirsung such as dilatation, tortuosity, single or multiple strictures, irregularity of the walls and calculi.

Etiology

Despite extensive and serious research it has not been possible to pinpoint the pathogenic role of any of the recognized and supposedly etiological factors associated with chronic pancreatitis. The clinical association between alcohol and chronic pancreatitis is well documented (34, 43, 52). In his comprehensive study of 733 patients with acute and chronic pancreatitis, White 1968 (81) found alcohol to be the main associated factor in 60% of the patients with a clear diagnosis of chronic pancreatitis. In a study covering 205 cases of confirmed acute, recurring and chronic pancreatitis respectively, Sarles 1965 (67) thoroughly investigated dietary and alcohol intake. In the group with chronic calcific pancreatitis, the daily alcohol intake was found to be twice as high as in the group with acute pancreatitis, and three times as high as in the

controls. It would seem that alcoholism is about as commonly associated with chronic pancreatitis as cholelithiasis traditionally is a concomitant of the acute form (80, 81). It should however, be pointed out that recent work by Kager 1972 (41) and Edlund 1977 (22) clearly shows that alcohol plays a dominant role also in acute pancreatitis, especially the more severe forms predominantly occurring in the male urban population.

Cholelithiasis is present to a varying degree in all published series of chronic pancreatitis. Except in the relatively few cases of stones impacted in the ampulla of Vater, it is difficult to evaluate whether cholelithiasis has been an etiological factor or a parallel phenomenon. The latter view is supported by Warren 1969 (78) observing the age-correlated discrepancy; the incidence of cholelithiasis rises with advancing age while that of pancreatitis reaches a peak between the fourth and fifth decade and rapidly declines thereafter. Other conditions recognized as related to chronic pancreatitis include hyperlipaemia (33), hyperparathyroidism (56) and an uncommon hereditary form (7, 30).

Considering all of the possible etiological factors mentioned above, about 15 per cent of patients with chronic pancreatitis remain without specific clinical correlation with other known disease. These cases must be classified as idiopathic (80). Thus, chronic pancreatitis still constitutes a complex clinical entity in which no solitary etiological agent has been isolated although several environmental and intrinsic factors contribute substantially.

PURPOSE AND PLAN OF THE PRESENT INVESTIGATION

The present thesis represents an epitome of a series of studies performed in an endeavour to arrive at optimal diagnostic and therapeutic management in patients with chronic pancreatitis. Since it is of such great importance to adjust surgical intervention closely to the pathological changes in the individual patient, diagnostic procedures must not only establish the nature of the disease, but also yield detailed information on the extent of the inflammatory changes, on ductal patho-morphology, on the degree of exocrine insufficiency and, if possible, exclude malignant lesions.

There is no single test which meets these demands so we must resort to a combination of several different procedures. The purpose of the studies, in this respect, was to obtain an effective sequence of diagnostic tests for routine practice, comparing the relative merits of available diagnostic methods.

Since conservative medical treatment in chronic pancreatitis has proved discouraging (40) several surgical procedures have been devised and advocated over the last twenty years (16, 79). The multiplicity of different methods elaborated is an indication that none has proved entirely satisfactory. Therefore, it should be of interest to evaluate the results of surgical treatment. This has also been one of our objectives.

METHODS

Diagnostic procedures

Pancreatic function was assessed by estimating trypsin levels in duodenal aspirates after a test meal as described by Lundh 1962 (49). A single lumen plastic tube was passed under fluoroscopic control, positioning the tip at the ligament of Treitz. Aspirates were collected in 10 minute aliquots during the first hour and in 30 minute aliquots during the second hour. They were immediately frozen to -20°C , at which temperature they were stored until analyzed. From each of the eight fractions 1 ml was withdrawn, shaken for 2 minutes and pooled. Within a week the trypsin activities of the pooled fractions were determined by automatic titration using para-toluene-L-arginine methyl ester (TAME) as substrate (36). Lipase activities were assayed as described by Erlanson and Borgström (23) and phospholipase as elaborated by Ihse and Arnesjö (37).

Before scintigraphic examination of the pancreas the patients were fasted for 12 hours. Twenty minutes before the i.v. injection of $200\ \mu\text{Ci}\ ^{75}\text{Se}$ -methionine, a standard proteinrich meal was given. After a further 20 minutes a static 25 minutes exposure was performed with the patient in the supine position and the collimator angled 20° cephalad. Thereafter a 2 minutes static exposure of the $^{99}\text{Tc}^{\text{m}}$ 140 keV photo peak was started, permitting electronic subtraction of overlapping hepatic tissue. This system is often useful although not always necessary. (The second ^{75}Se photo peak of 136 keV is virtually inseparable from the 140 keV photo peak of $^{99}\text{Tc}^{\text{m}}$ but the contribution is small enough to be negligible). A Searle Pho-gamma III camera carrying a medium energy collimator was used, connected to the digital Intertechnique Cine-scintigraphic system.

Angiographic examination was performed via the femoral arteries as selective catheterization of the coeliac and superior mesenteric arteries. Usually the contrast medium was injected simultaneously in both arteries. Superselective catheterizations of the hepatic and/or gastroduodenal artery was moreover carried out when considered necessary. The radiologic criteria used were those earlier described by Tylén (72, 73).

Intraoperative pancreatography was performed in some cases as a retrograde examination using the transampullary technique via a duodenotomy, cannulating the papilla as described by Trapnell 1966 (70). In the remainder the pancreatic tail was mobilized following splenectomy. After resection

of various amounts of caudal tissue, a polyethylene catheter (Intracath 16/17) was introduced 1-3 cm into the transected duct and fixed whereafter contrast medium was injected under low pressure. Films were exposed in frontal and oblique positions.

ERCP (endoscopic retrograde cholangio-pancreatography) was achieved through the Olympus JF-B or JF-B2 duodenoscope. After cannulation of the papilla of Vater and the injection of contrast medium the patient was rotated from semi-prone position, right side up, to the supine position whereupon films were exposed in various projections. Finally delayed pictures were taken to check the emptying process. The fate of injected contrast medium was closely observed fluoroscopically.

Surgical technique

Via a Puestow incision the duodenum and pancreatic head were mobilized and the gastroduodenal ligament divided. Following thorough examination of the pancreas and biliary tract the pancreatic tail and the spleen were mobilized en bloc. Splenectomy, amputation of the pancreatic tail and antegrade pancreatography was then performed in the majority of cases. In some instances the transampullary, retrograde technique was used. If isolated obstruction, undue widening or dislocation of the duct was found, end to side caudal pancreatico-jejunostomy was done (Fig. 1) (20). The transected pancreatic duct was kept patent by radial, absorbable sutures.

Where multiple stenoses or calculi were demonstrated, a longitudinal split, as suggested by Puestow and Gillesby 1958 (64) was performed, suturing the opened pancreatic duct partly side to side and partly inserted into a defunctionalized Roux-en-Y loop of the proximal jejunum (Fig. 2). All anastomoses were performed with double layer technique using interrupted sutures, the inner layer being absorbable.

Clinical evaluation

In the follow up studies (IV, V), the patients were summoned for personal interview, thorough clinical examination and routine laboratory tests. The subjective long term results were defined as *excellent*, *good*, *fair* and *poor* respectively. The over all result in each case represents a summary of several criteria such as general sense of well being, disappearance or relief of pain, improvement of nutritional state, resumption of work, need for continuous medication or re-hospitalization. An *excellent* result implies a practically complete freedom of symptoms while a *poor* result means no change from the preoperative state (IV).

A serious attempt was made to obtain a reasonably correct estimation of alcohol consumption. With regard to individual consumption the patients were referred to three sub-groups, thus symbolized: +++ = undisputable

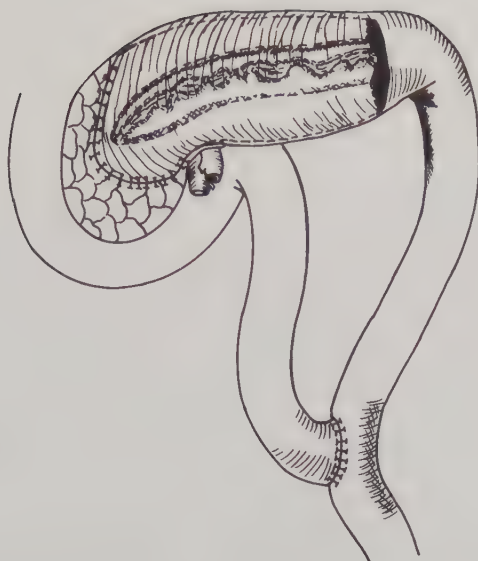


Fig. 1. The technique of caudal pancreatico-jejunostomy.

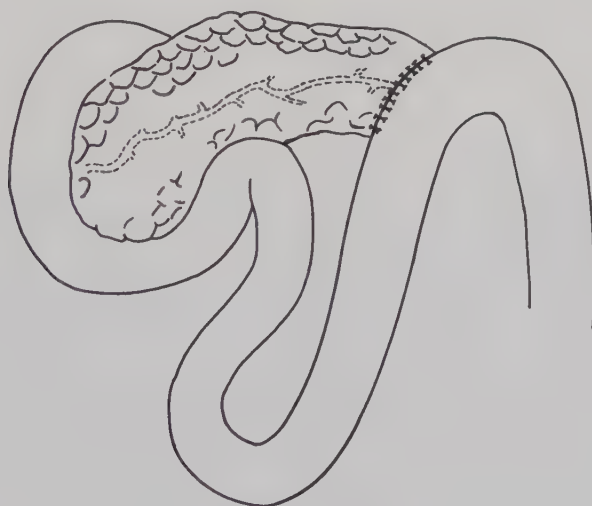


Fig. 2. The technique of longitudinal pancreatico-jejunostomy.
(Puestow-Gillesby).

alcoholism, ++ = moderate consumption, + = negligible intake.

DIAGNOSIS OF CHRONIC PANCREATITIS

Generally the clinical features in more advanced cases are quite clear-cut. Most patients present with a history of pronounced intermittent pain in the epigastrium, weight loss, gastro-intestinal disturbances, gallstones, alcoholism and varying degrees of addiction to analgesics or narcotics. In the less advanced and typical stages the symptoms may be extremely varied and are often diffuse. These patients present considerable diagnostic difficulties. Since routine laboratory tests and standard radiological examinations of the upper gastrointestinal tract often reveal nothing abnormal, more sophisticated diagnostic machinery is required.

When making a modern diagnostic approach to the pancreas, several paths may be entered. Of the non-invasive methods, ^{75}Se -methionine scintiscanning is the one where most global experience has accumulated (3, 4). Favourable results have recently been reported with ecotomography (25) and gray-scale ultrasonic scanning (11). Progress with computed tomography is also reported (31).

Of the pancreatic function tests the Lundh meal (49) is one of the most well known and widely used. It appears to yield diagnostic information fully comparable to the secretin test which involves hormonal pancreatic stimulation (50, 76). The determination of pancreatic iso-amylase in serum has recently been introduced as a new diagnostic tool (65).

As the above mentioned methods do not provide detailed information, invasive procedures such as selective angiography and ERCP, or in jaundiced patients PTC (percutaneous transhepatic cholangiography), may be utilized as a further step when planning appropriate surgical management and in excluding malignant infiltration. Because of the diagnostic problems that often arise in suspected pancreatic disease, it seemed important to establish the accuracy of available diagnostic procedures, comparing them and evaluating their relative merits. The Lundh pancreatic function test, pancreatic scintigraphy, selective angiography and intraoperative pancreatography (Wirsungiodiography) were selected for this evaluation mainly because these are the procedures most frequently performed in our patients during the last decade.

The value of Lundh pancreatic function test

Since it was designed in 1962, the Lundh test has been used all over the world in basically unaltered form. Favourable results with the method

are continuously reported (38, 42, 57, 77). In our comparative study (II), the test indicated pancreatic disease in 44 out of 49 patients with cancer or chronic pancreatitis, and acquitted the pancreas from disease in all patients where pancreatic engagement could later be excluded. In Fig. 3 the results of the Lundh test in chronic pancreatitis are shown in relation to those of scintigraphy and angiography.

It has been suggested by Goldberg and Wormsley (29) that the determination of more than one enzyme may be of value in pancreatic function tests, providing a means of double checking the enzyme excretory capacity. In our study comprising almost 500 patients (I), we found that the determination of trypsin alone (Lundh test) was helpful in the diagnosis of chronic pancreatic disease in 65 out of 74. The diagnostic accuracy was, however, found to be somewhat enhanced by the determination of enzyme constellations. Thus, in 9 of 98 patients with exocrine insufficiency the diagnosis would not have been obtained by the determination of trypsin or lipase as the sole enzyme.

Goldberg and Wormsley furthermore suggested that the ratios between the enzymes secreted might add diagnostic information. We found that the concentration ratios of lipase to trypsin (L/T) and to phospholipase (L/Ph) were different in health and disease (chronic pancreatic disease, coeliac disease and previous gastric resection), whereas the phospholipase to trypsin (Ph/T) ratio remained constant. It was, however, obvious that the variation between the individual patients was too great to permit of valid clinical conclusion.

Dreiling 1975 (19) has claimed a 90% success rate with the standard secretin test in distinguishing the abnormal pancreas from the normal. Our results with the Lundh test are fully comparable, as are those of several other workers (42, 50, 57, 76, 77). Furthermore, many find the secretin test impracticable and the results difficult to interpret while the Lundh test is a physiological and simple method with a very good reproducibility, inexpensive and well tolerated even by sick patients.

There are conditions however, in which the results of the Lundh test may be subnormal in a fairly high percentage of cases where the pancreas probably is normal. In our study of intestinal enzyme activities (I), we found subnormal trypsin concentrations after test meal stimulation in 9 patients out of 18 following Billroth II gastric resection, in 9 out of 29 patients with coeliac disease and in 5 out of 10 cases of severe diabetes mellitus. These factors are well known (38) and should be considered when applying the method.

Finally, it is our firm belief that none of the pancreatic function tests used today is capable of discriminating between neoplastic and inflammatory disease. As a screening test in suspected pancreatic disease, however, the Lundh meal is excellent and even better if more than one pancreatic enzyme is determined.

The value of pancreatic scintigraphy

In our comparative study (II), scintigraphy indicated pancreatic disease primarily, and on review without access to any clinical data, in 24 out of 24 patients with pancreatic cancer. In 25 patients with proven chronic pancreatitis, scintigraphy was positive in 24 cases primarily and in 23 on review. In the group with acute relapsing pancreatitis, scintigraphy was positive in 2 cases primarily and on review in a further 1, out of a total of 8 patients. In the last group, 16 patients with epigastric pains where pancreatic disease was later excluded, scintigraphy gave no primary false positives, but gave 1 on review.

Thus, out of a total of 49 patients with proven pancreatic disease, scintigraphy was positive in 48 out of 49 patients primarily and in 47 out of 49 on review, while in 16 patients where pancreatic disease was subsequently excluded, the scans were considered normal in all cases primarily and in 15 out of 16 on review. In 1 patient with pancreatic cancer scintigraphy was the sole positive test. These results stand up very well when compared to the other two methods evaluated (selective angiography and the Lundh test); they are also encouraging when compared to those of other workers (1, 45). In chronic pancreatitis and carcinoma, false-negative scans are not found in more than 4% (53). This is in accordance with our findings. Where false-positive results are concerned the evaluation presents a somewhat greater difficulty. In unselected patients, false-positive scans have been reported in 15-30% (6, 54). In some studies even higher rates are reported (47). Conditions found to cause false positive pancreatic scans include diabetes mellitus, hepatic cirrhosis, peptic ulcer, previous gastric surgery, ascites and obesity (3). If allowance for the aforementioned conditions is made, the rate of false-positive scans is acceptable, the remainder of "true" false positive scans occur in patients with duodenal trypsin levels near subnormal limits (2).

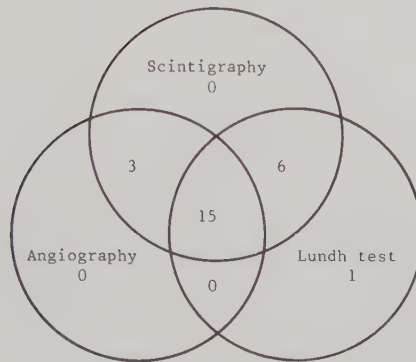
Although specific features in the abdominal scan of pancreatic carcinoma in that of chronic pancreatitis and in obstructive jaundice respectively have been reported (4), it is quite obvious that scintigraphy cannot attain the status of a specific diagnostic procedure.

In our opinion, providing that appropriate indications for pancreatic scintigraphy are appreciated, the method has a high level of diagnostic reliability and consistency in distinguishing the affected pancreas from the normal. Moreover, it has the advantage of being able to be performed on an out-patient basis, requiring no preparation and being painless and safe. A further advantage is the extra bonus of a simultaneous liver scan.

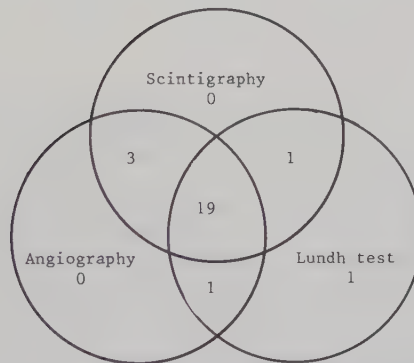
The value of selective angiography

When less hazardous methods, such as scintigraphy and the Lundh test indicate pancreatic disease, and when surgical procedures on the pancreas

Chronic relapsing pancreatitis (n = 25).



Pathologic diagnostic findings
primarily.



Pathologic diagnostic findings
on review.

Fig. 3. Comparison between results of angiography, scintigraphy and the Lundh test, primarily and on review in 25 patients with chronic relapsing pancreatitis. The sum of the figures within each circle represents the number of pathologic findings obtained using the respective method.

are contemplated, angiography is required for further detail knowledge.

In our comparative study (II), the diagnosis of pancreatic carcinoma was primarily overlooked angiographically in 4 out of 24 patients. In the group of 25 cases with chronic pancreatitis there were 7 false-negative results primarily. On review by a senior radiologist, these numbers were reduced to 1 and 2 cases respectively (Fig. 3). Thus, in chronic pancreatic disease in 49 patients, the false negative results were reduced from 11 instances to 3.

The difficulty in arriving at correct angiographic diagnosis has been pointed out by several workers (21, 26, 58). In a prospective series of patients with pancreatic carcinoma, Bookstein et al. (10) had false-negative angiographic results in 24%. Lunderquist (48), Boijesen (8) and Olsson (61) do however, report a high degree of accuracy in the diagnosis of pancreatic cancer. The differentiation between neoplastic and inflammatory disease is a major diagnostic problem requiring a thorough knowledge of the vascular changes in each of these conditions (9, 72, 73).

In their series of 87 patients with inflammatory disease of the pancreas in various stages, Tylén and Arnesjö 1973 (72) performed a thorough evaluation of characteristic intra- and extrapancreatic arterial and venous changes related to the type and phase of the disease. This study proved informative, showing that vascular changes wax and wane in relapsing pancreatitis in relation to the stage of the disease and to the number of acute attacks. Angiography also aids further encirclement of exact diagnosis, by serving as a guide for related techniques such as percutaneous fine needle biopsies (62, 74).

In conclusion the findings of our study (II) indicate that the accuracy of angiographic interpretation is somewhat dependent on subjective evaluation. Thus, the experience of the examiner appears to be a critical factor. The value of angiography is threefold, the differentiation between inflammatory disease and cancer, the mapping of vascular anatomy and the estimation of resectability of pancreatic malignancy. The method is obviously not suitable as a screening procedure in suspected pancreatic disease.

The value of pancreatography

Since Leger (44) introduced intraoperative pancreatography, several workers have concerned themselves with this issue (17, 32, 35, 70, 71). In our studies of relapsing pancreatitis (III, IV) the patients were referred to one of three subgroups according to the severity of inflammatory pancreatic changes present. A comparison between the gross findings at operation, the results of intraoperative pancreatography and of histopathologic examinations of resected specimens was performed. A fair correlation was demonstrated but in some cases a quite pronounced discrepancy was apparent.

The vast majority of the patients were operated upon with a clear diagnosis of chronic relapsing pancreatitis. Thus, the state of the pancreas indicated a decompressive shunt procedure in most of the patients for which reason the pancreatography was performed from the tail. The transduodenal procedure was performed in 6 cases but appeared to be afflicted with a high rate of complications, and should be reserved for cases where the duct proves difficult to localize via the tail or where the patient is subjected to duodenotomy for other reasons and where caudal pancreatico-jejunosomy is not contemplated.

It is quite obvious that a careful appreciation of the state of the duct of Wirsung is the basis for rational selective surgery. Since ERCP was put into practical use by Oi (1970) and Takagi (1970) (60, 68), its field of application has been continuously expanding (5, 14, 66). In modern diagnostic approach ERCP will probably replace the intraoperative techniques since it is less traumatic and yields more diagnostic information if correctly executed. Furthermore, ERCP is usually combined with a simultaneous cholangiogram and permits inspection of the duodenum and papillary region and the obtaining of biopsies and material for cytologic analysis. ERCP is however, a highly specialized form of procedure and only in the hands of a really experienced examiner will the cannulation success rate and the quality of the pancreatograms be as high as could be desired. Furthermore, there are conditions where the duodenal approach may be difficult, such as in stenosis of the papilla of Vater and after previous gastric (Billroth II) resections, distorted second part of the duodenum and in juxta-ampullary dicercicula (66). Considering these factors, intraoperative, antegrade pancreatography might still defend its place in the near future, as a valuable guide in selective surgery.

In summary, pancreatic scanning has been found to yield extremely few false-negative results (one out of 49 of the cases primarily, as compared to 11 out of 49 and 5 out of 45 for angiography and the Lundh test respectively). In proven disease of the pancreas the combination of scintigraphy and the Lundh test was positive in all of the cases. Similar results were reported by Youngs et al. 1973 (84). Our findings are furthermore in agreement with those of Mitchell et al. (55) and Ferruci and Eaton (24), recommending scintigraphy as an initial diagnostic step.

For additional detail information when differentiating neoplastic from inflammatory disease and when surgical intervention is contemplated, especially in carcinoma, angiography is indicated. It must be emphasized that this order of procedures is applicable only in the non-jaundiced patient. When obstructive jaundice of some standing is present, percutaneous transhepatic cholangiography (51, 75, 83) should be performed primarily, leaving the catheter to divert the bile externally. The drainage period may be used for additional investigations such as ERCP and angiography.

The results of the studies in the present thesis have led us to the following sequence of diagnostic procedures in suspected pancreatic disease;

1. First line procedures

Thorough case history and physical examination.

Routine laboratory tests.

Radiological examination of the upper gastro-intestinal tract and biliary system.

Gastroscopy.

2. Second line procedures

a/ Jaundiced patients.

PTC with an indwelling catheter to divert the bile if obstruction is encountered.

Directed fine needle biopsies during the cholangiographic examination, when so required.

b/ Non-jaundiced patients.

Determination of iso-amylase in serum.

Pancreatic function (Lundh) test.

Pancreatic scintigraphy.

Pancreatic ultrasonography.

3. Third line procedures

ERCP combined with endoscopic biopsy, cytologic examination of the pancreatic juice and percutaneous fine needle biopsy.

Angiography of the coeliac and superior mesenteric arteries, combined with percutaneous fine needle aspiration biopsy.

The sequence in non-jaundiced patients has jocularly been alluded to as the "3-stage diagnostic rocket" (Fig. 4).

This sequence of tests is at present in use at our hospital. In the future, however, it might be replaced by other sets of diagnostic methods. Our own experience with ultrasonography are encouraging but as yet too slender to permit definite conclusions. Swift progress is continuously made in the field of medical technology and diagnostic systems comprising combinations of Computed Tomography and Ultrasonography alone or in conjunction with ERCP are already tried and reported (15). Several of the new procedures, the merits of which still have to be assessed, will probably change the constitution of our whole diagnostic conception in the near future and accordingly modify the diagnostic scheme described above.

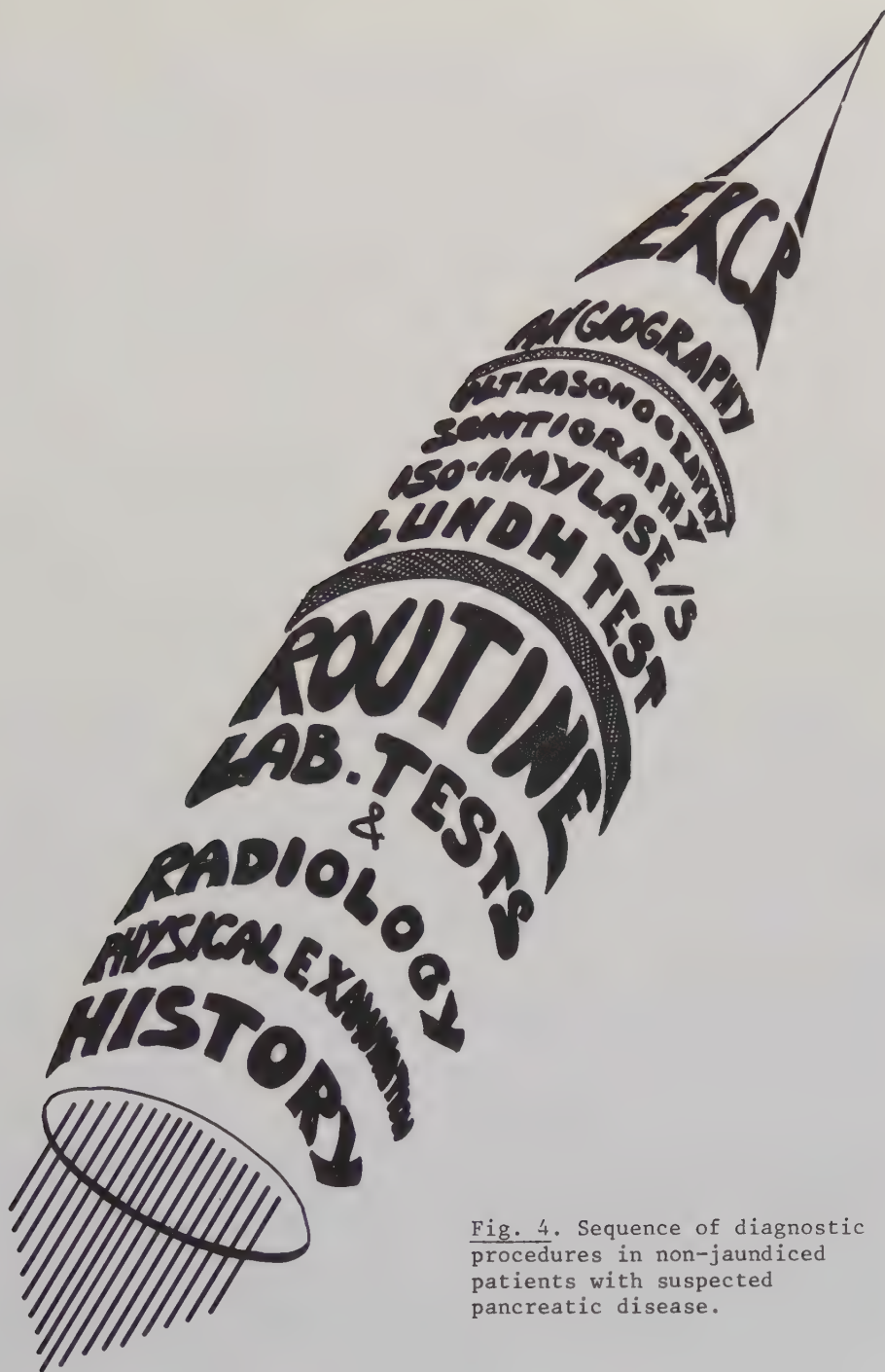


Fig. 4. Sequence of diagnostic procedures in non-jaundiced patients with suspected pancreatic disease.

SURGICAL TREATMENT OF CHRONIC PANCREATITIS

The multitude of suggested and elaborated surgical procedures in chronic pancreatitis, is an indication of our faulty knowledge of exact etiological mechanisms in a disease presenting extreme variations in clinical and pathological manifestations.

It is generally agreed however, that co-existing biliary disease should be corrected as an early measure in surgical management. Other indirect procedures attempted include sphincterotomy (18), vagotomy and pyloroplasty, subtotal gastrectomy, sympathetic denervation (59) and coeliac ganglionectomy (13). With the exception of corrective biliary surgery in the selected case, these procedures are purely palliative and have no influence on the course of the underlying disease.

In parallel with the development of pancreatographic technique, attention was focused on direct pancreatic surgery. A concept gaining wide acceptance postulated ductal obstruction to be a major factor in producing the severe pain which is the most distressing and common symptom in chronic pancreatitis. Pancreatography performed during surgery revealed pathologic ductal anatomy, often presenting single or multiple strictures in a vast majority of patients. With the intention of pain relief by alleviating pancreatic outflow from the obstructed duct, DuVal 1954 suggested resection of the pancreatic tail and caudal pancreatico-jejunosotomy (20). On account of the fact that multiple strictures were found to be a frequent phenomenon, Puestow and Gillesby 1958 designed the longitudinal split of the duct following splenectomy (64). In this manner a wider and longer anastomosis to the jejunum could be achieved. Partington and Rochelle (1960) and Thal (1962) (63, 69) modified the technique with the intention of preserving the spleen and the pancreatic tail (side to side pancreatico-jejunosotomy). In patients with changes restricted to the pancreatic head, a proximal resection may be performed (27, 79). Likewise, left side resections may be considered for well defined distal involvement. In severe pancreatitis without significant dilatation of the duct a 95% distal pancreatectomy has been recommended (28).

During the decade 1963 - 1973, 29 of the patients treated for chronic and acute relapsing pancreatitis at our hospital, were subjected to pancreatico-jejunosotomy. In order to evaluate the method, these patients were selected for an extensive clinical follow up study (IV).

The main indication for surgery had been severe pain and/or several attacks of clinically well-defined acute pancreatitis. Preoperative diagnosis was supported by exocrine pancreatic function tests, pancreatic scan and angiography, and verified intraoperatively by cytological examination of fine needle aspirates and antegrade pancreatography. Histo-pathologic examinations of the resected pancreatic tail specimens were performed in all cases. At follow up, a postoperative observation time was from 6 months to 10 years (mean 4 years).

The patients were divided into three groups according to the severity and extent of inflammatory changes at operation, as found on gross examination, pancreatography and histologic analysis. The diagnostic results obtained in the preoperative evaluation correlated well to these. In some patients however, the process was mainly confined to the ductal system as revealed by pancreatography, while in others the changes were most marked in the parenchyma as found at histological examination. The rate of postoperative complications was low; no mortality, one spontaneously healed anastomosis insufficiency. Subphrenic abscess developed in two instances. Long-term temperature rise and jaundice requiring re-operation with diverting choledocho-jejunostomy developed in one case.

Preoperatively, 5 patients had diabetes mellitus, this condition developed in a further 5 patients postoperatively. Endocrine and exocrine insufficiency has, however, not been a great problem to the patients in this series. One of the patients died 3 years postoperatively. At autopsy multiple abscess formation of the liver was found. Another patient succumbed 10 years postoperatively from a cerebral thrombosis, while in a third patient a carcinoma of the pancreas, unsuspected at operation, was diagnosed. This patient is still alive and well 2 years after diagnosis, receiving chemotherapy.

A total of 21 caudal pancreatico-jejunostomies and 8 longitudinal anastomoses were performed. Over all results were *excellent* (patients free of symptoms) in 20 cases. On a closer analysis of 9 cases where *excellent* results were not reported it was obvious that 7 were heavy drinkers. (Table I). In 6 of the cases, advanced inflammatory changes were noted on gross examination and histo-pathological analysis, while the ductal changes were only slight. Thus, the best results of drainage procedures in alcoholics are to be expected in cases presenting advanced ductal changes (Table I). That *excellent* results were not achieved in this group, might indicate that a substantial resection would have been a more appropriate procedure in these patients. Subtotal (95%), distal resection was advocated by Fry and Child (28). In a recent review (27) however, the authors state that sequelae to a 95% resection, such as the incidence and severity of diabetes, steatorrhea, peptic ulcer disease and the number of late deaths, reflect adversely on the method for control of pain. Desirable postoperative results were reported ranging around 50% after individually tailored right or left resections.

In a 20 year postoperative follow up study, Leger et al. (46) found a 50% long-term mortality in 16 patients subjected to pancreatico-duodectomy for chronic pancreatitis. Pancreatico-jejunostomy, performed in 45 cases, had rendered 49% pain-free while resection had relieved 54 out of 71 patients. Thus, resections appeared to be superior to drainage but the authors also found a 10% higher long-term mortality in the resection group.

White and Keith (82) followed up 50 patients after pancreatico-jejunostomy. Fourteen years postoperatively, 22 of the patients had died, 9 of these from a pancreatic carcinoma, unsuspected at operation. After a mean follow up period of 4 1/2 years, 46% of the patients were symptom-

free, 35% had improved while 19% were no better. The findings of this report further stress the known difficulty, in many cases, of differentiating between chronic inflammatory changes and malignancy by palpation. In one of our patients a cancer was possibly overlooked, despite the fact that needle biopsies were obtained from all clinically suspected areas of the pancreas during all these operations.

Jordan et al. (40) report a survey of results with different surgical methods in 1 558 patients from the recent American literature and a 20 year postoperative follow up study, of his own, in 30 patients treated with pancreatico-jejunostomy. Long-term results with the caudal anastomosis were reported as 50% excellent or improved, the corresponding figure for longitudinal pancreatico-jejunostomy being 70%. Thus, the results in our series, 26 out of 29 patients, reporting significant improvement postoperatively, are most encouraging, compared to those reported in contemporary literature.

Apart from the rewarding effect of pain relief, the operation almost entirely precluded further acute attacks of the disease. Accepting the theory that pain in chronic pancreatitis is partly due to pressure peaks in the obstructed excretory duct, a drainage procedure seems rational. To what extent the inflammatory process is modified by surgical intervention, is a matter of mere speculation. There is, however, some evidence (vide infra) that there is progress of those inflammatory changes that are reflected in ductal patho-morphology. Progression in spite of the operation was also seen at autopsies by Jordan (40).

Longitudinal pancreatico-jejunostomy then is a reasonably safe method, effective in relieving pain as a treatment for chronic relapsing pancreatitis where the duct of Wirsung is obstructed, dilated and/or containing concretions. Resections should be reserved for cases where the entire pancreas seems to be replaced by sclerotic tissue and where the ductal changes are discrete, or for cases where other procedures have not given the desired results.

In our entire series of 29 patients, alcohol intake was reduced in 4 cases while 4 patients had increased their consumption postoperatively. It should be mentioned that an extensive interview investigation of these patients was made independently of the hospital, by a group from the Institute of Sociology of the University of Lund. The results of this group regarding the patients' evaluation of postoperative results and their drinking habits, were almost identical with those presented to us (table I). Thus, the results of our investigation do not altogether lend support to the opinion that the pain-relieving effect of the operation is entirely dependant on a postoperative abstinence from alcohol.

From a social point of view, it is interesting to note that 20 out of 29 patients had resumed work at the time of follow up.

Table 1.

Comparison between postoperative results and ductal pathology based on intraoperative pancreatography and pre-/postoperative alcohol consumption in 8 patients subjected to the Puestow-Gillesby procedure and in 21 with caudal pancreatico-jejunostomy.

Postoperative results	Alcohol consumption pre-/postop.	Ductal pathology	Postoperative results	Alcohol consumption pre-/postop.	Ductal pathology
4	+++ / +++	+++	4	+++ / +	+++
4	+++ / +++	+++	4	++ / 0	++
4	+++ / +++	+++	4	++ / ++	+
4	+++ / ++	+++	4	++ / +++	+
4	+++ / ++	/	4	+ / +	+++
4	++ / +++	+++	4	+ / +	+
4	++ / +++	+++	4	+ / +	+++
3	+++ / +++	+++	4	+ / +	+++
			4	+ / +	+++
			4	0 / 0	+++
			4	0 / 0	+
			4	0 / 0	+
			4	0 / 0	/
			3	+++ / +++	+
			3	+++ / +++	+
			3	+++ / +++	+++
			3	+++ / +++	+
			3	0 / 0	+
			2	+++ / +++	+
			2	+++ / +++	++
			2	+ / ++	+

Postoperative results: 4 = excellent, 3 = good, 2 = fair, 1 = poor.

Alcohol consumption: +++ = alcoholic, ++ moderate consumption, + = negligible intake.

Pancreatography: +++ = marked dilatation, strictures, calculi, ++ = same type of changes but less pronounced, + = irregular walls or dislocation without significant dilatation.

FOLLOW UP OF SURGICAL TREATMENT

It is quite obvious that chronic pancreatitis, especially the sclerotic calcifying variety, is an alcoholic's disease. It appears that pancreatitis in the relapsing form predominantly occurs in a maladjusted and socially vulnerable clientele (43). Therefore, the surgical intervention must be regarded as a part of a comprehensive social rehabilitation programme in many of these patients. This requires a vivid interest in their social and personal problems apart from other re-adjustment measures. Frequent contacts with these patients may have a stabilizing effect on their postoperative course.

The general sense of well being of the patients postoperatively is, of course, the main decisive factor when evaluating results. Another factor is the positive influence of the operation on the number of acute attacks. There is, however, still a difficulty in objectivizing findings postoperatively with indirect methods. Exocrine function tests are usually omitted because of the technical difficulties in collecting pancreatic secretion from the shunted gland. Postoperative scintigraphies are also difficult to evaluate for which reason valid conclusions regarding the effect of the operation can not be drawn from them.

The introduction of ERCP represents a new approach in this field, making it possible to compare the clinical results with ductal patho-morphology and to compare the preoperative state of the duct with that at various intervals postoperatively. This idea led us to utilize ERCP as a part of follow up after pancreatico-jejunostomy. Thirteen patients were available for this study (V). In 4 of these patients a longitudinal anastomosis had been carried out while a caudal pancreatico-jejunostomy was performed in the remaining 9. Intraoperative pancreatographies had been done in all but one case (IV, III). These formed the bases of comparison. Mean observation time between intra- and postoperative pancreatograms was 3 years.

ERCP evidenced shunt patency in all cases with longitudinal anastomoses. In 2 of these patients progression of the inflammatory changes was noted; of the remaining 2 the short observation time did not allow any conclusions in 1 case, while intraoperative pancreatography had been omitted in the other. Signs of further progression were increased dilatation, irregularity and the formation of intraluminal concretions. Of these 4 patients, 3 admitted alcoholism postoperatively despite full information about the risks. They nevertheless claimed definite clinical improvement as a result of the operation, *excellent* in 3 cases, *fair* in 1. Of the 9 patients with caudal pancreatico-jejunostomy definite signs of progression of inflammatory ductal changes were noted in 6, in 5 of these intraluminal concretions had formed. In this group of 9 patients, shunt patency was evident in 1 case, uncertain in 2, while in the remaining 6 the examination suggested shunt occlusion. Of these 9 patients, 1 has ceased drinking alcohol altogether, 1 has reduced consumption considerably, 2 have increased their intake while the remaining 5 report unaltered drinking habits. In 6 of these patients post-

operative results were rated as *excellent*, in 2 as *good* and in one as *fair*.

The subjective postoperative results were thus unaltered at this stage of follow up as compared to the results of the earlier general follow up performed approximately 1 year previously (IV). Considering that so many of the caudal shunts seem to have occluded, it may be that the intraductal pressure has not been sufficient to keep them patent in these cases. In fact, all patients subjected to the less traumatic caudal shunt procedure, had slight stenosis or relatively minor changes evidenced in the intraoperative pancreatograms. The question arises whether these patients were wrongly selected for caudal pancreatico-jejunostomy. At present no answer can be given as our examinations only reflect the conditions at a given moment. It is unknown for how long the shunts remained patent postoperatively and the actual benefit hereof. Follow up with repeated postoperative ERCP examinations at controlled intervals in prospective studies will prove informative.

Somewhat contradictory to prevailing opinion are the facts that the results in the majority of patients were rated as *excellent* regardless of whether the shunts were patent or not and that these results appear to be independent of postoperative alcohol consumption.

It is also interesting to observe that the inflammatory changes appear to progress substantially even in cases where a well functioning drainage procedure has been carried out. There seems to be room for debate concerning the intraductal pressure peaks as the origin of pain, as well as the reversibility of inflammatory changes following appropriate drainage procedures in chronic relapsing pancreatitis.

CONCLUDING REMARKS

In a clinical study of almost 500 subjects, pancreatic function was studied using the Lundh test (I). In 88% of the cases with chronic pancreatic disease, the test was helpful. The study of concentration ratios between excreted enzymes indicated that calculation of ratios does not improve diagnostic accuracy, due to wide individual variations. The determination of enzyme constellations did however, per se, seem to improve the method to a certain degree. Since the Lundh test appears to be as reliable as the standard secretin test, it is justifiable to recommend it due to its practical advantages.

In a comparative study (II), pancreatic scintigraphy was also found to be a reliable method in indicating pancreatic disease. These two methods in combination were diagnostically helpful in all of our selected

patients with chronic pancreatic disease. The procedures have, however, not the capacity to differentiate between neoplastic and inflammatory disease of the pancreas. Thus, only when pancreatic disease is indicated with other methods, should selective angiography be performed for differentiation between cancer and pancreatitis preoperatively. It can also, to advantage, be combined with percutaneous fine needle biopsies. Furthermore, angiography is of great value in mapping vascular anatomy and in aiding assessment of extra-pancreatic pathological involvement when present. If malignancy is encountered, the procedure has proved helpful as a prognostic guide to resectability. On the basis of our evaluation of diagnostic procedures, a sequence of tests applicable in suspected pancreatic disease, has been proposed (Fig. 4).

In the near future, intraoperative pancreatography as a diagnostic procedure will probably be replaced by ERCP. We have, however, used the method to advantage as a guide to individual surgery in the selected case (III). Furthermore, due to pathologic changes in the duodenum and papillary region and to previous gastric surgery, ERCP may be difficult to perform. In these cases intraoperative, antegrade pancreatography will still be a useful method.

Postoperative follow up was performed in 29 cases operated upon with two types of pancreatico-jejunostomy for chronic pancreatitis (IV). In 20 of these patients the results were rated as *excellent*, as *good* in 6, as *fair* in 3 and as *poor* (no change) in none. Surgical intervention implied a drastic reduction of the number of acute attacks of pancreatitis in these patients. At follow up, 20 of the 29 patients had fully resumed their previous occupations. Postoperative alcohol consumption was not found to influence the results of surgery.

In a later follow up of postoperative results (V), 13 patients were subjected to ERCP. At the time of this examination, the pancreatico-jejunostomies were found patent in the 4 patients where the Puestow-Gillesby longitudinal anastomosis had been performed, while at least 6 of the caudal shunts were occluded.

Thus, accepting the theory that pain in chronic pancreatitis is caused by increased intraductal pressure, longitudinal pancreatico-jejunostomy appears to be the method of choice, offering the desired long term drainage. Caudal shunts have a tendency to become occluded losing their diverting function. The concept is supported by the fact that, of the 9 patients of our series of 29, in whom the results were not rated as *excellent*, 8 had been subjected to caudal pancreatico-jejunostomy.

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